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A Unique Subset: Idiopathic Intracranial Hypertension Presenting as Spontaneous CSF Leak of the Anterior Skull Base

Christopher S. Hong[1] Adam J. Kundishora[1] Aladine A. Elsamadicy[1] Eugenia M. Vining[2] R. Peter Manes[2] Sacit Bulent Omay[1]

[1] Department of Neurosurgery, Yale School of Medicine, Yale University, New Haven, Connecticut, United States
[2] Division of Otolaryngology, Department of Surgery, Yale School of Medicine, Yale University, New Haven, Connecticut, United States

Address for correspondence Sacit Bulent Omay, MD, Department of Neurosurgery, Yale School of Medicine, 20 York Street, LCI8, New Haven, CT 06511, United States (e-mail: sacit.omay@yale.edu).

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Abstract

Introduction Spontaneous cerebrospinal fluid (CSF) leaks represent a unique clinical presentation of idiopathic intracranial hypertension (IIH), lacking classical features of IIH, including severe headaches, papilledema, and markedly elevated opening pressures.

Methods Following a single-institution retrospective review of patients undergoing spontaneous CSF leak repair, we performed a literature review of spontaneous CSF leak in patients previously undiagnosed with IIH, querying PubMed.

Results Our literature review yielded 26 studies, comprising 716 patients. Average age was 51 years with 80.8% female predominance, and average body mass index was 35.5. Presenting symptoms included headaches (32.5%), visual disturbances (4.2%), and a history of meningitis (15.3%). Papilledema occurred in 14.1%. An empty sella was present in 77.7%. Slit ventricles and venous sinus stenosis comprised 7.7 and 31.8%, respectively. CSF leak most commonly originated from the sphenoid sinus (41.1%), cribriform plate (25.4%), and ethmoid skull base (20.4%). Preoperative opening pressures were normal at 22.4 cm H_2O and elevated postoperatively to 30.8 cm H_2O. 19.1% of patients underwent shunt placement. CSF leak recurred after repair in 10.5% of patients, 78.6% involving the initial site. A total of 85.7% of these patients were managed with repeat surgical intervention, and 23.2% underwent a shunting procedure.

Conclusion Spontaneous CSF leaks represent a distinct variant of IIH, distinguished by decreased prevalence of headaches, lack of visual deficits, and normal opening pressures. Delayed measurement of opening pressure after leak repair may be helpful to diagnose IIH. Permanent CSF diversion may be indicated in patients exhibiting significantly elevated opening pressures postoperatively, refractory symptoms of IIH, or recurrent CSF leak.

Keywords
- CSF leak
- anterior skull base
- intracranial hypertension
- pseudotumor

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Introduction

Spontaneous intracranial cerebrospinal fluid (CSF) leaks represent a unique clinical presentation of idiopathic intracranial hypertension (IIH), secondary to skull base erosion from chronically elevated CSF pressures.[1–5] IIH is typically diagnosed, based on the modified Dandy criteria,[6] among which include clinical signs and symptoms of increased intracranial pressure (ICP) (i.e., headache, visual disturbances), CSF opening pressures > 25 cm H_2O, and radiographic features on magnetic resonance imaging (MRI) such as an empty sella and venous sinus stenosis. In patients with CSF leak and a suspected underlying diagnosis of IIH, the leak may be a natural outlet of CSF egress in patients with chronically elevated ICPs. These patients may not develop or complain of the classical signs and symptoms of typical IIH at time of presentation. As such, we retrospectively reviewed our own recent institutional experience of management of spontaneous CSF leaks from anterior skull base defects and performed a literature review to further characterize patients presenting with spontaneous CSF leak from the anterior skull base and suspected but previously undiagnosed IIH.

Materials and Methods

We performed a literature search utilizing PubMed, querying the following search terms: spontaneous, cerebrospinal fluid leak, CSF leak, anterior skull base, meningocele, encephalocele, and intracranial hypertension. Articles reviewed were limited to those published in the past 50 years and written in the English language. Data collected included basic patient demographics (age, sex, body mass index [BMI]), presenting signs and symptoms, formal ophthalmologic findings, imaging features including presence of an empty sella, ventricular configuration, venous sinus stenosis, location of the CSF leak, presence of an cephalocele (defined as any of the following: meningocele, encephalocele, meningoencephalocele), opening pressure, and clinical outcomes including need for permanent CSF diversion. Studies that included spontaneous CSF leaks within a larger series of CSF leaks of other etiologies were only included if they contained additional information specific to the spontaneous CSF leak population, beyond basic demographic data. In addition, we collected similar data from a single-institution retrospective chart review of the last five patients treated for spontaneous CSF leak under an institutional review board-approved protocol.

Case Illustration

A 58-year-old obese woman presented to our institution's emergency department with complaints of clear fluid running from her nose and new-onset positional headaches, worse when upright, of 1-week duration. She denied any visual changes and was neurologically intact on examination, including no evidence of active CSF rhinorrhea. Computed tomography (CT) of the head revealed a thin acute subdural hematoma tracking along the falx and tentorium (►**Fig. 1A**). She exhibited a partially empty sella on brain MRI (►**Fig. 1B**).

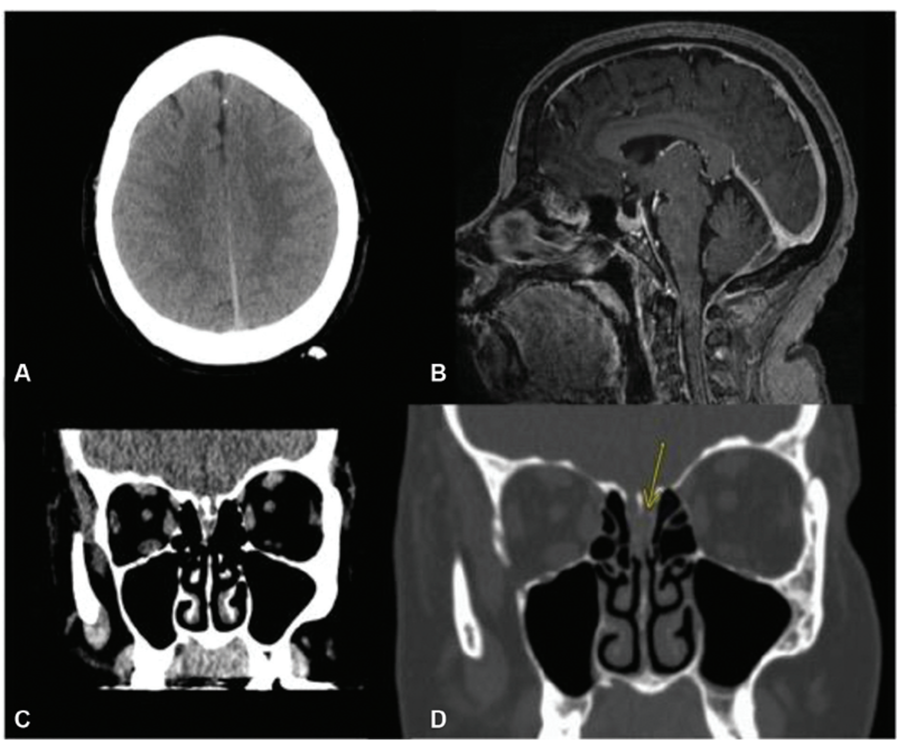

Fig. 1 (**A**) An axial slice from computed tomography (CT) of the head demonstrates a thin parafalcine subdural hematoma at time of presentation. (**B**) A sagittal image taken from T1-weighted brain magnetic resonance imaging (MRI) after gadolinium contrast administration shows a partially empty sella. (**C**) A coronal slice from a thin-cut CT of the head shows a boney defect of the right lamina papyracea with trace mucosal thickening in the right sphenoid sinus and left maxillary sinus. (**D**) Bone-windowing of the aforementioned image shows soft tissue or fluid immediately subjacent to the cribriform plate bilaterally, inferior to the olfactory bulb region in the olfactory recess of the nasal vault (arrow), suggestive of a bony defect in the left cribriform plate.

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Thin-cut slices from a skull base CT revealed an anterior skull base defect, accompanied by a meningocele (►**Fig. 1C, D**). Vascular imaging ruled out stenosis or thrombosis of the venous system, and ophthalmologic examination did not demonstrate evidence of papilledema. After admission, she developed recurrent rhinorrhea, and fluid was sent for β-2-transferrin testing, which confirmed CSF. She subsequently underwent endonasal endovascular repair of her CSF leak, aided by use of intrathecal administration of fluorescein via preoperative lumbar drain placement, to localize the area of leak to the lateral cribriform plate. Postoperatively, her opening pressure measured via the lumbar drain was 14 cm H_2O, which was subsequently removed after 2 days of drainage, and she was discharged on acetazolamide. However, 6 weeks after CSF leak repair, she developed recurrent headaches, despite lack of recurrent CSF rhinorrhea and continued acetazolamide therapy. A repeat lumbar puncture was performed, revealing an opening pressure of 29 cm H_2O. Subsequently, she was counseled and elected to undergo ventriculoperitoneal shunt placement and experienced immediate and continued resolution of her symptoms at 6-month follow-up. The clinical history of this patient (patient 1) and the other four patients in our institutional case series are summarized in ►**Table 1**.

Results

Patient Demographics

Our review of the literature yielded 26 total studies, including our own patient cohort, comprising a total of 716 patients meeting criteria for presentation of spontaneous CSF leak from the anterior skull base without prior history of IIH (►**Table 1**). The average age of the patients was 51 years, 80.8% female predominance, and an average BMI of 35.5. Out of the 22 studies reporting clinical symptoms, those besides complaints of rhinorrhea at time of presentation included significant headaches (164/504, 32.5%) and subjective visual disturbances (21/504, 4.2%). A history of meningitis, whether remote, acute, or otherwise not specified was reported in 77/504 patients (15.3%). Out of 142 patients from 11 studies who underwent formal ophthalmologic examination, papilledema was reported in 20/142 or 14.1% of patients.

Radiographic and Intraoperative Findings

Studies were further analyzed for imaging and intraoperative characteristics of the patient population, based on available data provided on a study-by-study basis (►**Table 2**). A partial or fully empty sella was described in 271/349 (77.7%) patients, derived from 15 studies. Out of 39 patients from 5 studies with descriptors or available imaging of ventricular configuration, only 3 (7.7%) exhibited slit ventricles. Venous sinus stenosis was reported in 21/66 (31.8%) patients from 6 studies. The primary location of the CSF leak was reported in 24 studies and originated from the sphenoid sinus (272/662, 41.1%), cribriform plate (168/662, 25.4%), ethmoid bone (135/662, 20.4%), frontal sinus (47/662, 7.1%), planum sphenoidale (10/662, 1.5%), optic canal (2/662, 0.3%), and other (9/662, 1.4%; i.e., maxillary sinus, lateral anterior skull base, clivus, or unknown). An additional 19/662 (2.9%) leaks originated from the temporal bone. However, this study did not aim to capture leaks of middle fossa origin, so these patients were only included because they were a part of a larger series of spontaneous CSF leaks involving the anterior skull base. A cephalocele was present in 277/351 (78.9%) of patients, derived from 22 studies.

CSF Dynamics

The average opening pressure among 446 patients from 14 studies prior to surgical repair of their CSF leak, was 22.4 cm H_2O, excluding a single case of an opening pressure of 320 cm H_2O due to fulminant bacterial meningitis.[7] In addition, 250 patients from 9 studies underwent measurement of their opening pressure after CSF leak repair, which averaged 30.8 cm H_2O. Among 539 patients from 22 studies reporting need for permanent CSF diversion for their CSF leak, 103 (19.1%) subsequently underwent shunt placement (►**Table 1**).

Recurrence Rates

Patterns of CSF leak recurrence and their management were further analyzed. Recurrence rates in larger case series ($> n = 20$) ranged from 2.9 to 22%.[8–17] Excluding five studies with insufficient data, the overall recurrence rate was 10.5% (56/535 patients). Within this group, 44 (78.6%) recurred at the same site, while the remaining 12 (21.4%) recurred at a distant site. Time to recurrence at the same site (range: postoperative day 2 to 15 months) tended to occur earlier than at a distant site (range: 8 months to 9 years).[8–11,14,15] Overall, 48/56 (85.7%) patients with recurrent leaks were managed with repeat surgical intervention, among who 13 (23.2%) patients also underwent shunt placement.[9,14–16,18,19] Three patients were managed conservatively with temporary CSF diversion in the form of a lumbar drain.[13,14,20] Three patients developed recurrent leaks, secondary to shunt malfunction and subsequently underwent shunt revision surgery.[15,19,21] Three patients with recurrent leaks within days after initial repair were managed with repeat surgery without need for a further shunting procedure.[9,10,22]

Discussion

While the relationship between spontaneous CSF leaks and an underlying diagnosis of IIH has long been recognized within the neurosurgery and otorhinolaryngology literature, this study sought to confirm our own institutional experience with literature experience, regarding distinct clinical and radiographic features differentiating these patients from those with a typical presentation of IIH. Demographically, we found that patients with spontaneous CSF leaks with a suspected but previously undiagnosed history of IIH were generally older than typically reported ages of patients with newly diagnosed IIH but otherwise still demonstrated a preponderance of obese females among the patient population, consistent with the IIH literature.[1,23,24] Additionally, we found a lower prevalence of headache and subjective visual disturbances in these patients, consistent with larger case series[9,10,14] that have reported lower rates than those in

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Table 1 Summary of institutional case series

	Age/ gender	BMI	Presenting symptoms	Pre- and postoperative ophthalmology findings	Imaging findings	Location of CSF leak	Opening pressure (cm H_2O)	Immediate postoperative outcome	Clinical management	Last follow-up
Patient 1	58/F	41	2 wk of severe headaches, rhinorrhea	Normal No postoperative f/u	Thin parafalcine subdural hematoma, empty sella, meningocele; normal ventricles, normal venous sinuses	Ethmoid	14 (perioperatively), 29 (3 mo postrepair)	Continued headaches, fatigue w/o recurrent leak	Acetazolamide followed by ventriculoperitoneal shunt placement 3 mo postrepair with cessation of acetazolamide	9 mo: No recurrence of leak, resolution of headaches, and improved subjective mentation
Patient 2	47/F	27	6 wk of headaches, rhinorrhea	Normal Normal (7 mo postrepair)	Empty sella, meningocele; normal ventricles, congenitally narrowed L transverse-sigmoid sinus	Sphenoid	26 (1 mo postrepair)	Continued headaches, fatigue w/o recurrent leak	Acetazolamide dose doubled, neurovascular consultation for potential stenting but patient did not want further invasive interventions	7 mo: No recurrence of leak, resolution of headaches
Patient 3	55/M	37	4 wk of headaches, rhinorrhea History of spontaneous R otorrhea with R mastoid repair 8 y prior	Normal Normal (2 mo postrepair and shunting)	Empty sella, expanded Meckel's cave, bilateral optic nerve sheath dilation; normal ventricles, normal venous sinuses	Ethmoid	19 (1 wk postrepair)	Worsening nonpositional headaches, complaints of recurrent rhinorrhea prompting representation to ED 1 wk postrepair	Acetazolamide followed by ventriculoperitoneal placement 2 wk postrepair after worsening symptoms with cessation of acetazolamide	2 mo: Headaches resolved after shunt placement and further dialing down of shunt
Patient 4	56/F	37.5	2 y of intermittent rhinorrhea, lifelong headaches	Normal Normal (8 mo postrepair)	Empty sella, meningocele normal ventricles, normal venous sinuses	Ethmoid	TBD	No further leak	Acetazolamide but causing intermittent paresthesias	3 mo: No recurrence of leak, improvement of headaches; awaiting measurement of opening pressure
Patient 5	53/F	39	Acute bacterial meningitis, rhinorrhea, lifelong headaches	Normal No postoperative f/u	Empty sella, meningocele; normal ventricles, normal venous sinuses	Cribriform	22 (2 mo postrepair)	No further leak, persistent headaches	Acetazolamide	6 mo: No recurrence of leak, persistent headaches diagnosed as migrainous, occipital neuralgia and relieved with topiramate and nerve block

Abbreviations: BMI, body mass index; CSF, cerebrospinal fluid; TBD, to be determined.

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Table 2 Summary of studies reporting spontaneous anterior skull base CSF leak in patients with suspected IIH

Study	Number of patients	Average age (y)	Gender (% female)	BMI (kg/m^2)	Symptoms besides leak	Prevalence of papilledema (proportion of evaluated patients, %)	Imaging features (proportion of evaluated patients, %)	Presence of cephalocele (proportion of evaluated patients, %)	Location of CSF leak	Average opening pressure (cm H_2O)	Treatment with shunt (n, %)	Recurrence rates postrepair (proportion of evaluated patients, %)	Prevalence of local recurrence (proportion of evaluated patients, %)
Clark et al, 1994[2]	4	38.3	4 (100%)	NR	Headache (3), Visual disturbances (2)	3/4 (75%)	Slit ventricles (2/4, 50%)	NR	Cribriform (4)	32	3 (75%)	None	None
Lopatin et al, 2003[11]	21	NR	15 (71.4%)	NR	Meningitis history (11)	NR	NR	10/21 (47.6%)	Cribriform (6), Ethmoid (6), Sphenoid (9)	NR	0 (0%)	1/21 (4.8%)	1/1 (100%)
Schlosser et al, 2006[51]	16	49.6	13 (81.3%)	35.9	Headache (10), Tinnitus (5), Visual disturbances (2)	0/3 (0%)	Empty sella (11/11, 100%), Sinus stenosis (0/11, 0%)	16/16 (100%)	Sphenoid (12), Ethmoid (6), Cribriform (2), Frontal (2)	26.5	3 (27.3%)	None	None
Woodworth et al, 2008[8]	56	61	43 (77%)	36.2	Meningitis history (10)	NR	Empty sella (42/49, 85%)	54/56 (96%)	Sphenoid (30), Ethmoid (17), Cribriform (12), Frontal (7)	27 (48 patients)[a]	13 (21.3%)	6/56 (11%)	3/6 (50%)
Banks et al, 2009[17]	77	51.4	57 (74%)	35.4	Headache (8), Meningitis history (31)	NR	NR	70/77 (91%)	Sphenoid (31), Ethmoid (23), Cribriform (16), Frontal (9), Other (1)	NR	12 (16%)	7/77 (9%)	4/7 (57.1%)
Seth et al, 2010[9]	39	57.5	33 (84.6%)	38.5	Headache (17), Tinnitus (5), Visual disturbances (4)	3/39 (9.4%)	Empty sella (24/39, 77.4%)	33/39 (84.6%)	Cribriform (21), Sphenoid (14), Ethmoid (3), Frontal (1)	24	6 (15.4%)	5/39 (12.8%)	5/5 (100%)
Ramakrishnan et al, 2011[41]	16	NR	9 (56.3%)	NR	NR	NR	NR	9/16 (56.3%)	NR	26, 15[a]	NR	NR	NR
Pérez et al, 2013[21]	3	41.3	2 (67%)	NR	Meningismus (1), Headache (2), Visual disturbances (1)	1/3 (33%)	Empty sella (⅔, 66%), Sinus stenosis (⅓, 33%)	2/3 (66%)	Cribriform (2), Sphenoid (1)	37.5	3 (100%)	1/3 (33.3%)	1/1 (100%)
Rosenfeld et al, 2013[3]	4	42.3	4 (100%)	34.8	Headache (2), Visual disturbances (1)	4/4 (100%)	Slit ventricles (¼, 25%)	3/4 (75%)	Cribriform (3), Temporal (1)	NR	2 (50%)	None	None
Aaron et al, 2014[37]	16	52	14 (87.5%)	43	NR	0/17 (0%)	Sinus stenosis (1/16, 6.3%)	NR	Planum (5), Ethmoid (3), Cribriform (3), Sphenoid (4), Optic nerve sheath (1)	27.4, 36.0[a]	4 (25%)	NR	NR
Chaaban et al, 2014[19]	46	51.2	32 (69.6%)	35.6	Meningitis history (4)	NR	Empty sella (35/46, 85.4%)	45/46 (98%)	Frontal (20), Sphenoid (18), Cribriform (14), Ethmoid (10), Planum (4), Optic nerve sheath (1)	24.3, 32.3[a]	20 (43.5%)	5/46 (10.9%)	4/5 (80%)
Chang, 2014[55]	1	47	1 (100%)	NR	None	NR	Empty sella (1/1, 100%)	1/1 (100%)	Cribriform (1)	NR	0 (0%)	None	None
Illing et al, 2014[56]	59	52	48 (81%)	36	NR	NR	Empty sella (44/59, 74.6%)	56/59 (94.95%)	Sphenoid (59)	27.7	NR	NR	NR
Melo et al, 2014[22]	6	47.2	6 (100%)	NR	Headache (3), Meningitis history (1)	NR	Empty sella (¼, 25%)	4/6 (66%)	Sphenoid (6)	NR	2 (33%)	1/6 (16.7%)	1/1 (100%)
Marston et al, 2015[18]	1	48	1 (100%)	26	None	0/1 (0%)	Empty sella (1/1, 100%)	0/1 (0%)	Sphenoid (1)	17	1 (100%)	1/1 (100%)	0/1 (0%)
Campbell et al, 2016[15]	32	54.2	28 (88%)	36.8	NR	NR	NR	31/32 (96.9%)	Sphenoid (18), Ethmoid (12), Cribriform (9), Frontal (4), Unknown (1)	27.7	7 (21.9%)	7/32 (22%)	3/7 (42.9%)
McCorquodale et al, 2016[7]	1	63	1 (100%)	NR	Headache (1)	NR	Slit ventricles (0/1, 100%)	1/1 (100%)	Sphenoid (1)	320	NR	NR	NR
Aaron et al, 2017[54]	63	51.7	57 (90.5%)	39.4	NR	NR	NR	NR	NR	25.9	NR	NR	NR
Iyer et al, 2017[39]	2	56.5	1 (50%)	30.4	Headache (1)	0/2 (0%)	Empty sella (2/2, 100%), Sinus stenosis (2/2 100%)	2/2 (100%)	Planum (1), Temporal (1)	23.2, 26.9[a]	0 (0%)	None	None
Martínez-Capoccioni et al, 2017[10]	35	62	25 (71.4%)	35.4	Headache (28), Tinnitus (18), Imbalance (14), Visual disturbances (2)	NR	Empty sella (27/35, 77.1%)	24/35 (68.5%)	Cribriform (18), Ethmoid (15), Sphenoid (2)	33	0 (0%)	1/35 (2.9%)	1/1 (100%)
Jiang et al, 2018[14]	48	51.4	45 (94%)	35.8	Headache (24), Meningitis history (7), Visual disturbances (2), Tinnitus (2)	2/28 (7.1%)	Empty sella (12/25, 48%), Slit ventricles (0/25, 0%)	NR	Sphenoid (23), Cribriform (16), Ethmoid (8)	22.5[a]	3 (6.3%)	9/48 (18.8%)	9/9 (100%)

(*Continued*)

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Table 2 *(Continued)*

Study	Number of patients	Average age (y)	Gender (% female)	BMI (kg/m^2)	Symptoms besides leak	Prevalence of papilledema (proportion of evaluated patients, %)	Imaging features (proportion of evaluated patients, %)	Presence of cephalocele (proportion of evaluated patients, %)	Location of CSF leak	Average opening pressure (cm H_2O)	Treatment with shunt (*n*, %)	Recurrence rates postrepair (proportion of evaluated patients, %)	Prevalence of local recurrence (proportion of evaluated patients, %)
Khafagy et al, 2018[13]	40	39.6	35 (87.5%)	36.7	Headache (33), Visual disturbances (6), Meningitis history (4)	NR	Empty sella (28/40, 70%)	19/40 (47.5%)	Ethmoid (19), Cribriform (14), Sphenoid (5), Frontal (2)	26.6	0 (0%)	4/40 (10%)	4/4 (100%)
Bidot et al, 2020[16]	36	50	34 (94%)	36.8	Meningitis history (1)	7/36[a] (19.4%)	Empty sella (27/29, 93.1%), Sinus stenosis (17/29, 68%)	26/29 (90%)	Ethmoid (10), Sphenoid (10), Frontal (2), Temporal (14)	22.5[a]	5 (14%)	6/36 (16.7%)	5/6 (83.3%)
Hanz et al, 2020[20]	17	45.9	11 (64.7%)	28	Headaches (15), Meningitis history (3)	NR	NR	17/17 (100%)	Sphenoid (17)	NR	2 (11.8%)	1/17 (5.6%)	1/1 (100%)
Kreatsoulas et al, 2020[12]	46	52.2	37 (80.4%)	39.8	Headaches (16), Meningitis history (3)	NR	NR	28/46 (60.9%)	Cribriform (26), Sphenoid (10), Other (7), Temporal (3)	30.4[a]	15 (32.6%)	2/46 (4.3%)	2/2 (100%)
Index study	5	54	3 (60%)	36.3	Headaches (2), Visual disturbances (1), Meningitis history (1)	0/5 (0%)	Empty sella (5/5, 100%), Slit ventricles (0/5, 0%), Sinus Stenosis (0/5, 0%)	3/5 (60%)	Ethmoid (3), Sphenoid (1), Cribriform (1)	24[a]	2 (40%)	None	None

Abbreviations: BMI, body mass index; CSF, cerebrospinal fluid; IIH, idiopathic intracranial hypertension; NR, not reported.
[a]Opening pressure measured after surgical repair of CSF leak.

typical IIH patients.[25] Together, these observations likely reflect a slower natural history of progressive intracranial hypertension in patients with spontaneous CSF leak, that may act as a "pressure release valve"[1] and relieve symptoms of elevated ICP, leading to later age at presentation and diminished acuity of related symptoms. Although the exact pathophysiology linking spontaneous CSF leak with IIH remains unclear, the most prevalent explanation is related to chronic erosion of the skull base secondary to elevated ICPs, eventually precipitating CSF leak.[26] Along these lines, others have proposed additional disorders related to skull base defects, associated with IIH, including cephalocele development and dehiscence of the cerebral venous–glymphatic system where they make contact with the skull base, secondary to intrinsic dural defects.[5,27,28] However, why only a subset of patients with IIH go on to develop spontaneous CSF leaks remains unclear.

Radiographic findings of IIH typically include a partial or empty sella, reported in up to 80% of patients with IIH.[29] Our literature review showed a lower prevalence of this finding in patients with spontaneous CSF leak, consistent with a pooled prevalence of 60%, cited in a previous literature review.[1] Slit ventricles are another radiographic feature, which have been classically associated with IIH.[30–32] While more recent studies incorporating MRI have not recapitulated this finding, slit ventricles remain a highly specific radiographic finding in IIH.[33] Our literature review found that the vast majority of patients with spontaneous CSF leaks do not exhibit slit ventricle morphology, perhaps further supporting the notion that consideration of ventricular configuration is irrelevant in the diagnosis of IIH with or without CSF leak. Notably, transverse sinus stenosis was found to be the most specific radiographic sign of IIH with also high sensitivity.[33] Out of the studies analyzed in our literature review, nearly a third (31.8%) of patients who underwent radiographic evaluation of the venous sinus system demonstrated evidence of stenosis that could be contributing to IIH physiology. However, venous imaging was only performed in 6 of the 26 studies analyzed in this review, including our own patient series, and as such, it remains unclear whether its prevalence in spontaneous CSF leaks is due to true pathophysiology versus underreporting. Venous sinus stenosis has been well-described in the general IIH literature, and a recent literature review of endovascular venous sinus stenting for IIH[34] reported improvement or resolution of IIH symptoms, including headaches, visual acuity, papilledema, and tinnitus in over 70% of patients. As such, venous sinus stenting has been advocated for in classic IIH patients with persistent symptoms, refractory to medical management and with elevated opening pressures and pressure gradients across the stenosis.[35] At our institution, we routinely obtain preoperative magnetic resonance venography (MRV) and will refer patients to the neurovascular service for possible endovascular stenting if the patient exhibits subjective (i.e., persistent headaches, visual disturbances) or objective (i.e., elevated opening pressures, new papilledema) signs of IIH postrepair.

Our literature review also showed that only 14.1% of patients demonstrated papilledema, diagnosed by ophthalmologic evaluation, in patients presenting with spontaneous CSF leak.

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This finding is consistent with the notion of the CSF leak acting as a pressure release valve, preventing long-term sequelae of chronically elevated ICPs, such as papilledema or optic nerve atrophy. Bidot et al confirmed this in 36 patients with pre- and postoperative neuro-ophthalmologic evaluations, demonstrating that only 4 (13.3%) had optic nerve changes consistent with previously undiagnosed IIH.[16] Furthermore, only one patient developed new papilledema postrepair. Likewise, Jiang et al found that only 2/28 (7.1%) of patients developed papilledema after repair of their CSF leak, correlating with delayed measurements of postoperative opening pressures.[14] At our institution, all of our patients are evaluated by neuro-ophthalmology prior to surgery and ideally within 3 to 6 months postrepair, a timeline consistent with previous studies.[14,16] In our small case series, none of our patients who had postoperative ophthalmology follow-up exhibited new abnormalities. While uncommon, new ophthalmologic deficits postrepair are a likely indication for shunting since this finding has been rarely reported without other signs of IIH such as worsening symptoms or recurrent CSF leak. As such, we routinely perform a postoperative neuro-ophthalmology evaluation, as development of new optic nerve changes, particularly while on acetazolamide therapy, would lead us to pursue counseling the patient on shunt placement.

While elevated ICP of over 25 cm H_2O constitutes part of the Dandy criteria to diagnose IIH and has also been described as the threshold for defining elevated opening pressures based on large population-based studies,[6,36] it is unclear whether ICP measurements can be applied to diagnosing underlying IIH in patients presenting with spontaneous CSF leaks. The natural presumption would be that ICPs may be normal in these patients, particularly if measured after clinical leakage of CSF.[37] In extreme cases, the change in ICP gradient could even provoke intracranial hemorrhage, as observed in patient 1 of our case series, presumably due to some degree of intracranial hypotension. Interestingly, we found in our literature review that among studies reporting opening pressures that were obtained prior to CSF leak repair, the average ICP measurement was 22.4 cm H_2O, constituting a normal value for IIH diagnosis according to the Dandy criteria and population-based studies. This was not unexpected given that chronic recurrent CSF leaks in patients with underlying IIH pathology have been proposed to act as a "pressure valve"[1] or means to normalize elevated ICPs. This likely contributes to attenuation of typical IIH symptoms, and as a consequence, delayed age at time of presentation. Furthermore, among the studies we reviewed, larger cohorts consistently reported average opening pressures below 25 cm H_2O.[9,14,19,38] In contrast, large-scale studies of classical IIH have typically reported opening pressures over 30 cm H_2O, including the Idiopathic Intracranial Hypertension Treatment Trial, which remains the largest randomized controlled trial of IIH conducted to date.[24,39,40] Given the conflicting data in the literature, we have moved away from considering preoperative opening pressures, measured at time of lumbar drain placement to guide postoperative management. Instead, we now routinely obtain postoperative opening pressures ideally 1 month after repair.

Among studies reporting opening pressures obtained after CSF leak repair, the average ICP elevated to 30.8 cm H_2O, which is not surprising given after successful surgical repair, the lack of CSF egress may increase ICPs due to elimination of the pressure valve and exacerbate an underlying condition of IIH.[19] Additionally, among those studies in our review reporting both pre- and postrepair opening pressures in their patient cohorts, there were consistent increases in ICP measurements,[19,39] aside from one study, which observed decreases in ICPs postrepair, albeit only measured 2 days after surgery.[41] Interestingly, these elevations in ICPs after CSF leak repair were only modest and still below the typical opening pressures over 30 cm H_2O, observed in IIH patients without CSF leak. However, this finding should be interpreted with caution, given these values were derived from a heterogeneous group of studies with varying methodologies to measure ICPs after CSF leak repair. Notably, Chaaban et al found in their larger cohort of 46 patients that ICPs significantly increased from a baseline of 24.3 cm H_2O preoperatively to 32.3 cm H_2O within days after CSF leak repair,[19] highlighting the notion that CSF leak repair may rapidly alter ICP dynamics and potentially precipitate typical IIH symptoms in the postoperative period. Indeed, we observed this with patient 3 in our case series who underwent shunt placement 1 week after his repair, despite a normal opening pressure, due to development of severe nonpositional headaches. His headaches completely resolved after shunt placement. Some authors have described measurement of ICPs, 1 to 2 days after surgery with a lumbar drain, to guide decision-making in starting acetazolamide therapy or same-admission shunting for moderately elevated and significantly elevated (i. e., $>$ 30–35 cm H_2O) opening pressures.[12,37] At our institution, we typically remove the lumbar drain at the end of the case or in select cases with larger defects, within 24 to 48 hours postoperatively, to facilitate early mobilization and discharge planning. We perform a lumbar puncture to measure opening pressure ideally 1 month after surgery, which allows for recovery from surgery while giving patients a period of time to self-monitor for development of classical IIH symptoms.

Spontaneous CSF leaks have reportedly had higher rates of recurrence after repair than leaks of other etiologies.[42] Presumably, this is due to a failure to treat the underlying elevated ICPs in this patient population after leak repair, leading to recurrence at the original or a distant site.[43] The patients who experienced recurrent CSF leaks, secondary to failure of their shunts, placed after their initial repair are a proof-of-concept of this principle. In a meta-analysis of recurrence rates after primary endoscopic repair of spontaneous CSF leaks, Teachey et al found that patients who underwent ICP measurement and intervention postrepair (with acetazolamide or permanent CSF diversion with a lumboperitoneal or ventriculoperitoneal shunt) had higher rates of long-term success (92.82%) than those with no ICP intervention (81.87%) at a mean follow-up of approximately 2 years.[43] Our review of the literature yielded a comparable overall recurrence rate of 10.5% with the additional finding that local recurrences tended to occur earlier after repair than distant ones.[15,16] Local recurrences are likely due to lack of identifying and treating the underlying IIH postrepair,[19]

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while distant recurrences may be from predisposed remodeling of the skull base from chronically elevated ICPs, emphasizing the importance of long-term follow-up.[28,44] We found that the vast majority (85.7%) of patients with leak recurrences were managed with a second surgery, regardless of whether the leak was local or distant. All patients with immediate recurrences (i.e., within days after repair) were managed successfully with repeat surgery, which likely reflected a failure of the repair itself rather than due to rapid onset of postoperative elevated ICPs. In contrast, nearly one-quarter (23.2%) of patients underwent an additional shunting procedure, typically for elevated ICPs ($>$ 25 cm H_2O), measured at time of leak recurrence, or in the setting of acetazolamide cessation, both reflecting underlying IIH pathophysiology.[15,16,19]

Given the risk of recurrence, the management of suspected IIH in patients after repair of their CSF leak is crucial, but practice patterns vary greatly. Although weight loss is routinely recommended, significant weight loss is typically required, including over 10 kg in one patient that led to gradual resolution of her papilledema,[3] which can be challenging for many patients and has often required bariatric surgical intervention in patients with classical IIH.[45] Interestingly, Sanghvi et al found that despite significant weight loss counseling but no change in BMI, most patients did not experience recurrence of preoperative IIH symptoms after CSF leak repair.[46] While we routinely refer high BMI patients for weight loss counseling after surgery, we have not observed any cases of BMI normalization contributing to resolution of IIH symptoms. Several studies in our literature review utilized acetazolamide in the postoperative period after CSF leak repair.[10,19,37] Despite the known ICP lowering effects of acetazolamide,[24] our literature review revealed that its application to these patients with suspected IIH after CSF leak repair is still on a case-by-case basis. Some groups have advocated for its use only after documenting elevated opening pressures after CSF leak repair,[9,12] while others have administered it prophylactically for at least 6 months, regardless of ICP measurements in the postoperative period.[10] Furthermore, indefinite acetazolamide therapy may be appropriate in certain individuals, as there have been reports of recurrent CSF leak in the setting of stopping acetazolamide.[19,21] While acetazolamide's side effects include vomiting, diarrhea, debilitating fatigue, dysgeusia, and paresthesias,[47–49] these are generally dose-dependent[50] and we have found most patients to tolerate acetazolamide well. Unless there is a clear alternative etiology for the CSF leak (i.e., prior trauma or tumor surgery to the skull base), we empirically treat an underlying IIH pathophysiology after leak repair with a relatively low dose of acetazolamide (250 mg three times daily) as a preventative measure against recurrent leak or development of IIH symptoms, even if the documented opening pressure postrepair is normal. In fact, patient 2 in our case series was successfully managed with increased dosing of acetazolamide for persistent headaches and fatigue after repair, after she declined further invasive interventions in the form of shunting or endovascular sinus stenting. However, as patient 4 demonstrated with development of intermittent paresthesias, the side effects of acetazolamide may preclude long-term use in some patients, necessitating consideration of further treatment options. Permanent CSF diversion in the form of shunting may be considered for cases of significantly elevated opening pressures postoperatively, recurrent CSF leak, and/or failure of medical therapies to treat IIH symptoms. However, there is no consensus on the indications for shunt placement for patients after repair of their spontaneous CSF leak with suspected underlying IIH diagnosis. Among the studies we reviewed reporting postrepair outcomes, we found that 19.1% of patients ultimately underwent permanent CSF diversion via shunt placement. Typically, indications for shunt surgery were development of classical IIH symptoms post-CSF leak repair (i.e., headaches, visual disturbances) and/or objective evidence of elevated ICPs such as elevated opening pressures ($>$ 30 cm H_2O) and papilledema.[21,38,51] Others reported shunt placement to manage persistent CSF leaks after multiple repairs, despite modest opening pressures or lack of development of typical IIH symptoms,[9,18] and in select cases, prior to undergoing CSF leak repair in patients with definitive signs of IIH.[21] We have utilized elevated postoperative opening pressures in the setting of ongoing acetazolamide use to be an indication for shunt placement. Although our experience is limited, we have anecdotally found that after going shunt placement for elevated opening pressures postrepair (patient 1) or severe recurrence of IIH symptoms (patient 3), both patients reported a subjective sense of significantly improved clarity of mentation, compared with their baseline status prior to developing spontaneous CSF leak.

Based on this literature review and our preliminary institutional experience, we have developed an algorithm for which we manage patients with spontaneous CSF leak and a suspected underlying diagnosis of IIH (►**Fig. 2**). All patients at time of presentation undergo MRV, in addition to routine CT and MRI for preoperative planning. In addition to neurosurgery and otolaryngology evaluations, patients are referred for baseline neuro-ophthalmologic testing. At time of surgery, a lumbar drain with fluorescein injection is utilized to help localize the site of the leak and is typically removed at the end of surgery. Postoperatively, patients are started on acetazolamide therapy, which is continued indefinitely unless they experience intolerable side effects or undergo a shunt procedure. Patients with evidence of preoperative venous sinus stenosis are referred to the neurovascular service for consideration of sinus stenting. An opening pressure measured via lumbar puncture is typically obtained 1 to 2 months after surgery, as well as a repeat neuro-ophthalmology evaluation within several months postrepair. Our indications for shunt placement thus far have included an elevated (i.e., $>$ 25 cm H_2O) postoperative opening pressure or persistence of IIH symptoms postrepair, despite acetazolamide therapy. Additionally, in accordance with the literature, we would suggest that recurrent CSF leak or new optic nerve changes be strong indications for consideration of shunt placement. The management of asymptomatic patients with elevated postoperative opening pressures may be particularly challenging. While most of the literature has demonstrated that these patients are typically monitored for developing signs of IIH, we found it striking that the

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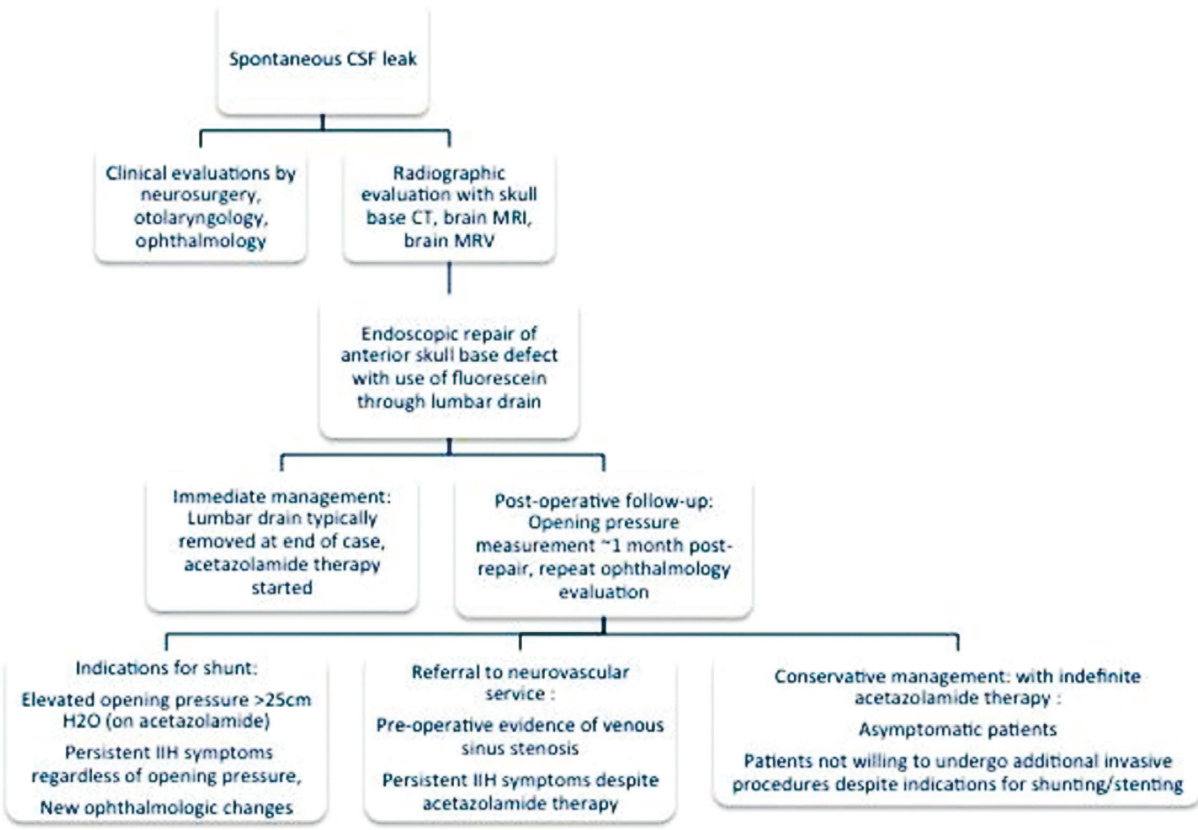

Fig. 2 Schematic detailing a proposed algorithm for management of patients with spontaneous cerebrospinal fluid (CSF) leak of the anterior skull base and a suspected underlying diagnosis of idiopathic intracranial hypertension (IIH).

two patients we shunted reported drastic improvements in mentation compared with their baseline status prior to any development of headaches or CSF leak. Further reports are needed to determine whether upfront shunting may be beneficial in asymptomatic patients with elevated postoperative opening pressures despite conservative treatments and weighed against the known risks of shunt malfunction or infection.

This study has several key limitations. Its retrospective nature reflects a highly heterogeneous group of studies that varied in the extent of describing the clinical and radiographic characteristics of the reported patients. Consequentially, it is difficult particularly to draw conclusions on the optimal management of these patients, both at time of presentation and after surgical repair of their CSF leak. Additionally, this study was confined only to spontaneous CSF leaks of the anterior skull base. Spontaneous CSF leaks, associated with underlying IIH pathophysiology, are also well-known to arise within the middle and posterior fossa,[4,52,53] and we suspect there is overlap of their management, particularly after surgical repair, with the findings discussed in this review. However, we chose to limit our literature review to anterior skull base defects, based on our institutional experience of combined neurosurgery and otolaryngology involvement for anterior skull base defects only. Given the potential risk of concurrent leaks in the mastoid or lateral skull base, these areas should be carefully evaluated in patients presenting with rhinorrhea, particularly if there are otologic complaints or findings of serous otitis media. In addition, our literature review was observational, and while the data were contrasted to the existing literature of IIH, no direct comparisons could be made with use of statistical analyses. Retrospective studies like Aaron et al,[37,54] comparing IIH patients presenting with spontaneous CSF leak to matched IIH controls with typical presentation are valuable and would be increasingly impactful on a larger scale. Moreover, a prospective study of patients with spontaneous CSF leak that includes measurement of ICPs at time of presentation and after repair, formal radiographic evaluation, and monitoring for development of symptoms of classical IIH and need for further intervention may be optimal and likely is not beyond the realm of feasibility.

Conclusion

An underlying diagnosis of IIH must be strongly suspected in patients presenting with spontaneous CSF leaks. Our experience and review of the literature suggest that these patients may present differently from typical IIH patients, including absence of a significant headache history and lack of subjective or objective evidence of visual deficits. Opening pressures may be predominantly normal, reflective of attenuation of intracranial hypertension via the CSF leak. In addition, in contrast to slit ventricle morphology characteristic of typical IIH, imaging in these patients may reveal a normal ventricular configuration, as

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well as an empty sella, the latter reflective of long-standing undiagnosed IIH. While medical therapy with acetazolamide for IIH is commonplace, definitive treatment via permanent CSF diversion or venous stenting may be indicated in patients exhibiting significantly elevated opening pressures postoperatively, developing signs of classical IIH, or experiencing recurrent CSF leaks.

Conflict of Interest
None declared.

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